This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 21-54 are pending.

1-20. (Canceled)

21. **(Previously Presented)**A non-human transgenic animal having a transgene integrated into the genome of the animal and also having a *tet* operator-linked gene in the genome of the animal, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the animal operatively linked to a polynucleotide sequence encoding a fusion protein which activates transcription of said *tet* operator linked gene,

the fusion protein comprises a first polypeptide which is a mutated Tet repressor that binds to a *tet* operator sequence in the presence of tetracycline or a tetracycline analogue operatively linked to a second polypeptide which activates transcription in eukaryotic cells,

said transgene is expressed in cells of the animal at a level sufficient to produce amounts of said fusion protein that are sufficient to activate transcription of the let operator-linked gene; and

in the presence of tetracycline or a tetracycline analogue in the animal, said fusion protein binds to the *tet* operator-linked gene and activates transcription of the *tet* operator linked gene such that the *tet* operator-linked gene is expressed at detectable levels, wherein the level of expression of the *tet* operator-linked gene can be downmodulated by depleting tetracycline or a tetracycline analogue from the animal.

22. **(Previously Presented)** A non-human transgenic animal having a transgene integrated into the genome of the animal and also having a *tet* operator-linked gene in the genome of the animal, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the animal operatively linked to a polynucleotide sequence encoding a fusion protein which inhibits transcription of said *tet* operator linked gene,

the fusion protein comprises a first polypeptide which is a mutated Tet repressor that binds to a *tet* operator sequence in the presence of tetracycline or a tetracycline analogue operatively linked to a second polypeptide which inhibits transcription in eukaryotic cells,

said transgene is expressed in cells of the animal organism at a level sufficient to produce amounts of said fusion protein that are sufficient to inhibit transcription of the *tet* operator-linked gene; and

in the presence of tetracycline or a tetracycline analogue in the animal, said fusion protein binds to the *tet* operator-linked gene and inhibits transcription of the let operator linked gene, wherein the level of expression of the *tet* operator-linked gene can be upregulated by depleting tetracycline or a tetracycline analogue from the animal.

23. **(Previously Presented)** A non-human transgenic animal having a transgene integrated into the genome of the animal organism and also having a *tet* operator-linked gene in the genome of the animal, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the animal operatively linked to a polynucleotide sequence encoding a fusion protein which inhibits transcription of said let operator linked gene,

said fusion protein comprises a first polypeptide that is a Tet repressor, operably linked to a heterologous second polypeptide which inhibits transcription of said *tet* operator-linked gene in eucaryotic cells,

said transgene is expressed in cells of the animal at a level sufficient to produce amounts of said fusion protein that are sufficient to inhibit transcription of the *tet* operator-linked gene; and

in the absence of tetracycline or a tetracycline analogue in the organism, said fusion protein binds to the *tet* operator-linked gene and inhibits transcription of the *tet* operator linked gene, wherein the level of expression of the let operator-linked gene can be upregulated by administering tetracycline or a tetracycline analogue to the animal.

24. **(Previously Presented)** The animal of claim 21, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.

25. **(Previously Presented)** The animal of claim 24, wherein the mutated Tel repressor is a mutated Tn10- derived Tet repressor having an amino acid substitution at at least one amino acid position selected from the group consisting of position 71, position 95, position 101 and position 102.

26. **(Previously Presented)** The animal of claim 24, wherein the mutated Tn10-derived Tet repressor comprises an amino acid sequence shown in positions 1 to 207 of SEQ ID NO: 2.

27. **(Previously Presented)** The animal of claim 21, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

28. **(Previously Presented)** The animal of claim 22, wherein the second polypeptide of the fusion protein comprises a transcriptional silencer domain of a protein selected from the group consisting of v-erbA, the Drosophila Krueppel protein, the retinoic acid receptor alpha, the thyroid hormone receptor alpha, the yeast Ssn6/Tup1 protein complex, the Drosophila protein even-skipped, SIR1, NeP1, the Drosophila dorsal protein, TSF3, SF1, the Drosophila hunchback protein, the Drosophila knirps protein, WT1, Oct-2.1, the Drosophila engrailed protein, E4BP4 and ZF5.

29. **(Previously Presented)** The animal of claim 21, wherein expression of the transgene is regulated by at least one let operator sequence.

30. **(Previously Presented)** The animal of claim 21, wherein expression of the transgene is regulated by at least one virally-derived regulatory element.

31. **(Previously Presented)** The animal of claim 21, wherein expression of the transgene is regulated by at least one tissue-specific regulatory element.

32. **(Previously Presented)** The animal of claim 21, wherein the let operator-linked gene is a second transgene comprising a gene of interest operably linked to at least one *tet* operator sequence.

33. **(Previously Presented)** The animal of claim 32, wherein the at least one *tet* operator sequence is operatively linked upstream of the second transgene.

34. **(Previously Presented)** The animal of claim 32, wherein the at least one *tet* operator sequence is operatively linked downstream of the second transgene.

35. **(Previously Presented)** The animal of claim 21, wherein the *tet* operator-linked gene is an endogenous gene that has been operatively linked to at least one *tet* operator sequence.

36. **(Previously Presented)** The animal of claim 21, which is selected from the group consisting of: a goat, a cow, a sheep, a monkey, a dog, a cat, a rabbit, a rat, or a pig.

37. **(Previously Presented)** A transgenic non-human animal whose genome comprises a transgene comprising a transcriptional regulatory element functional in cells of the transgenic non-human animal operatively linked to a polynucleotide sequence encoding a fusion protein,

said fusion protein comprising a first polypeptide which is a Tet repressor operatively linked to a second polypeptide which directly or indirectly activates transcription of a *tet* operator linked gene such that the transgenic non-human animal has detectable levels of the *tet* operator linked gene in one or more cell types or tissues of the transgenic non-human animal.

38. **(Previously Presented)** The transgenic non-human animal of claim 37, wherein the Tet repressor is a mutant Tet repressor.

39. **(Previously Presented)** The transgenic non-human animal of claim 38, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.

40. **(Previously Presented)** The transgenic non-human animal of claim 38, wherein the mutated Tet repressor is a mutated Tn10- derived Tet repressor having an amino acid substitution at at least one amino acid position selected from the group consisting of position 71, position 95, position 101 and position 102.

41. **(Previously Presented)** The transgenic non-human animal of claim 38, wherein the mutated Tn 10-derived Tet repressor comprises an amino acid sequence shown in positions 1 to 207 of SEQ ID NO: 2.

42. **(Previously Presented)** The transgenic non-human animal of claim 37, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

43. **(Previously Presented)** The animal of claim 37, which is selected from the group consisting of a mouse, a goat, a cow, a sheep, a monkey, a dog, a cat, a rabbit, a rat, or a pig.

44. **(Previously Presented)** A transgenic non-human animal whose genome comprises a *tet* operator-linked gene and a transgene comprising a transcriptional regulatory element functional in cells of the transgenic non-human animal operatively linked to a polynucleotide sequence encoding a fusion protein which activates transcription of the *tet* operator linked gene,

said fusion protein comprising a first polypeptide which is a Tet repressor operatively linked to a second polypeptide which directly or indirectly activates transcription in eukaryotic cells,

wherein said transgene is expressed in cells of the transgenic non-human animal at a level sufficient to produce amounts of said fusion protein that are sufficient to activate transcription of the let operator-linked gene at detectable levels in the absence of tetracycline or a tetracycline analogue.

45. **(Previously Presented)**A transgenic non-human animal whose genome comprises

a *tet* operator-linked gene and

a transgene comprising a transcriptional regulatory element functional in cells of the transgenic non-human animal operatively linked to a polynucleotide sequence encoding a fusion protein which activates transcription of the let operator linked gene,

said fusion protein comprising a first polypeptide which is a mutated Tet repressor operatively linked to a second polypeptide which directly or indirectly activates transcription in eukaryotic cells,

wherein said transgene is expressed in cells of the transgenic non-human animal at a level sufficient to produce amounts of said fusion protein that are sufficient to activate transcription of the *tet* operator-linked gene at detectable levels in the presence of tetracycline or a tetracycline analogue.

46. **(Previously Presented)** The transgenic non-human animal of claim 45, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.

47. **(Previously Presented)** The transgenic non-human animal of claim 46, wherein the mutated Tet repressor is a mutated Tn10- derived Tet repressor having an amino acid substitution at at least one amino acid position selected from the group consisting of position 71, position 95, position 101 and position 102.

48. **(Previously Presented)** The transgenic non-human animal of claim 46, wherein the mutated ml 0-derived Tet repressor comprises an amino acid sequence shown in positions 1 to 207 of SEQ ID NO: 2.

49. **(Previously Presented)** The transgenic non-human animal of claim 44, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

50. **(Previously Presented)** The transgenic non-human animal of claim 45, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

51. **(Previously Presented)** A transgenic non-human animal whose genome comprises

a *tet* operator-linked gene and

a transgene comprising a transcriptional regulatory element functional in cells of the transgenic non-human animal operatively linked to a polynucleotide sequence encoding a fusion protein which inhibits transcription of the *tet* operator linked gene,

said fusion protein comprising a first polypeptide which is a Tet repressor operatively linked to a second polypeptide which directly or indirectly inhibits transcription in eukaryotic cells,

wherein said transgene is expressed in cells of the transgenic non-human animal at a level sufficient to produce amounts of said fusion protein that are sufficient to inhibit transcription of the *tet* operator-linked gene.

52. **(Previously Presented)** The transgenic non-human animal of claim 51, wherein the second polypeptide of the fusion protein comprises a transcriptional silencer domain of a protein selected from the group consisting of v-erbA, the Drosophila Krueppel protein, the retinoic acid receptor alpha, the thyroid hormone receptor alpha, the yeast Ssn6/Tupl protein complex, the Drosophila protein even-skipped, SIRI, NeP1, the Drosophila

dorsal protein. TSF3, SF1, the Drosophila hunchback protein, the Drosophila knirps protein, WTI, Oct-2.1, the Drosophila engrailed protein, E4BP4 and ZFS.

53. **(Previously Presented)** The transgenic non-human animal of claim 51, wherein the Tet repressor is a mutant Tet repressor.

54. **(Previously Presented)** The animal of claim 51, which is selected from the group consisting of a mouse, a goat, a cow, a sheep, a monkey, a dog, a cat, a rabbit, a rat, or a pig.